
"During the war need arose to investigate synthetic mydriatics which might be used in place of atropine if supplies of the latter became inadequate. Synthetic atropine was thought to present a far too difficult manufacturing problem and the only synthetic mydriatic of the atropine type in common use, viz. eucatropine, is a much less powerful drug. The supply of homatropine is, of course, dependent upon the same sources as atropine. . . . The practical outcome of the work . . . was the discovery of a synthetic mydriatic, benzilipoxyethyl dimethylethalammonium chloride, which has been referred to so far as E3, but which it is proposed to name lachesine . . . While it is unlikely that lachesine will replace atropine in normal times, it may well prove to be a valuable addition to the armoury of the ophthalmic surgeon both as a short-acting mydriatic and cycloplegic, and for the treatment of patients who are allergic to the belladonna alkaloids." 18 references.

J.C. M. C.


"Until the 19th century, the remedies used in medical practice were either inorganic mineral salts or crude extracts from plants. As the study of organic chemistry progressed, these crude extracts were analyzed, their active constituents were isolated and their constitution determined. From this the next step was to try to synthesize these substances in the laboratory from such materials as coal tar, etc., and a further step was taken when attempts were made to improve on nature by altering the formula of a substance slightly and so enhancing its therapeutical effects. . . . A very good ex-

ample of the progressive steps leading to the discovery of a new remedy is the work which led to the introduction of aspirin. . . . The earliest record of the production of an entirely synthetic remedy was the synthesis of chloral by Liebig in 1832. . . . Up till the end of the 18th century only crude extracts of opium were available, but in 1816 Sertürner described the isolation of the most potent of the opium alkaloids, morphine. Subsequently 5 other alkaloids were isolated, namely codeine, thebaine, papaverine, and nareine. Narcotine had previously been isolated by Derosne. . . . One very undesirable property shared by all the phenanthrene alkaloids of opium is the liability to cause addiction. Drug addiction became such a serious problem in the United States that a special committee was set up to try to find synthetic analogues for morphine which would reproduce the analgesic properties without the undesirable side-effects. Since there appeared to be a definite relationship between chemical structure and biological activity, it was thought that the best way to tackle the problem would be to try to find out if possible what parts of the morphine molecule are specific for its different effects. . . . The first approach made was to try the effect of substitutions in the groups attached to the phenanthrene nucleus, and in particular the phenolic and alcoholic OH groups. . . . A further method that was tried was that of nuclear substitution. . . . Yet another method was to start, not from the morphine molecule itself, but from the simple phenanthrene nucleus, or from some other nucleus, such as dibenzofuran or carbazol. . . . Another group of workers (Dodds, Lawson and Williams, 1944) approached the problem from a rather different angle. Bearing in mind that stilboestrol, which bears only loose chemical relationship to the naturally-occurring oestrogens, is able to replace these in every way, these
workers considered the possibility that synthetic analogues might be found for other naturally-occurring substances containing the phenanthrene ring system. As a starting point diphenylethylamine was tested, and then 17 derivatives of this were prepared and investigated. . . . Five of the compounds, M3, M4, M2, M7, and M18, were tested clinically. For this purpose they were administered orally to patients suffering from pain due to malignant disease and who were having morphine at 4-hourly intervals. The substances to be tested were substituted for the morphine without informing the patient. Substances, M2, M7 and M18, were found to be inactive. M3, when given in doses of 200 mg. every 3 hours, was found to relieve the pain, but mental confusion developed after about one hour. When given to normal persons, M3 produced elation and slight muscular incoordination. M4 was tried on 14 patients and gave complete relief of pain in all cases without any signs of mental confusion or undesirable after-effects. Extensive clinical investigation, however, showed that this series of compounds relieved only pain associated with nerve-pressure. They were found to be completely effective in cases of carcinomatous growth pressing on nerves, but appeared to be without any activity on pain caused by inflammatory processes and similar conditions. It must, of course, also be emphasized that substances of this series at present investigated are of only theoretical interest, and are not suitable for adoption into clinical practice. It may well be, however, that further investigations in this series would succeed in producing substances of actual clinical importance."

3 references.

J. C. M. C.


"The recognition of a group of cases of contact dermatitis, apparently clearly linked to the handling of narcotics in a wholesale drug company’s factory, appeared to be a rather ordinary problem. . . . The realization that we had under our care a group with largely identical findings made it seem worthy of publication as evidence of the more widespread dissemination—existing in a possibly different factory environment in America—of an irritant capable of causing a persistent and refractory dermatitis. . . . It was given us as a rough estimate that about 60 employees were engaged in one or other of the special tasks involving contact with morphine or codeine during the year covering the cases detailed in this report. Some of these persons—all of whom were white and, with one exception, women—speedily developed irritation from the material and, on changing their duties, as rapidly showed off the effects of exposure. Others persisted, became ‘hardened’ to the irritant, and were able to continue. Still others were never affected. One worker had been intimately exposed to morphine products for twenty-seven years without any ill effects; others gave records of similar service from three to ten years. Definitely the drug is not a primary irritant, but nevertheless one which finds many persons susceptible to its local effect upon the skin.

"The number of mild cases disposed of by the non-medical supervisors or plant medical attendants was not known with certainty, but it undoubtedly formed a considerable proportion. . . . The reason for the rather abrupt onset of incidence of these cases of dermatitis—for the industrial process had been conducted in this manner for some years—seemed to be clearly linked to war-time emergency and speed-up. Whereas the various alkaloids had